

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY**

**IN RE BENICAR (OLMESARTAN)
PRODUCTS LIABILITY
LITIGATION**

MDL No. 2606

Master Case No. 15-2606 (RBK/JS)

Hon. Robert B. Kugler, U.S.D.J.

Hon. Joel Schneider, U.S.M.J.

THIS DOCUMENT RELATES TO
ALL CASES

**DEFENDANTS' REPLY BRIEF IN RESPONSE TO PLAINTIFFS'
OPPOSITION AND IN FURTHER SUPPORT OF DEFENDANTS'
MOTION TO EXCLUDE THE TESTIMONY OF PLAINTIFFS' EXPERT
STEPHEN LAGANA, M.D.**

DRINKER BIDDLE & REATH LLP

A Delaware Limited Liability Partnership

600 Campus Drive

Florham Park, New Jersey 07932-1047

(973) 549-7000

Attorneys for Defendants Daiichi Sankyo,
Inc., Daiichi Sankyo US Holdings, Inc.,
Daiichi Sankyo Company, Ltd., Forest
Laboratories, Inc., now known as Forest
Laboratories, LLC, Forest Pharmaceuticals,
Inc., and Forest Research Institute, Inc.

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INTRODUCTION

To determine whether testimony from Plaintiffs' expert Dr. Stephen Lagana is admissible, the Court must first assess the methodology underlying that testimony. As demonstrated below, Dr. Lagana's methodology is flawed to the point that it is unreliable. Accordingly, for the reasons set forth below and in Defendants' motion, Dr. Lagana's opinions should be excluded.

ARGUMENT

A. Dr. Lagana's inability to define sprue-like enteropathy, criteria for a diagnosis, and general causation are grounds for excluding his general causation opinion.

A determination of whether expert testimony is admissible requires a preliminary assessment of whether the methodology underlying the testimony is scientifically valid. *See Daubert v. Merrill Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 592-93 (1993); *see also Lithuanian Commerce Corp. Ltd. v. Sara Lee Hosiery*, 177 F.R.D. 245, 261 (D.N.J. 1997). None of the allegations that Plaintiffs throw against Defendants' recitation of Dr. Lagana's testimony salvage the flaws inherent in his methodology, which remains unreliable. Plaintiffs accuse Defendants of falsely stating that Dr. Lagana opined that any gastrointestinal problem that improves after olmesartan is discontinued falls within the diagnosis of sprue-like enteropathy. (Pls.' Br. at 5, Dkt. 1106). They argue that because Dr. Lagana ruled out a hypothetical case of abdominal pain as not being sprue-like

enteropathy, Defendants' statement is inaccurate. Not so.

In fact, Dr. Lagana testified that he considers a case of abdominal pain as non-classical and is "not sure that [he] would put that particular label [of sprue-like enteropathy] on it." Dr. Lagana's carefully phrased words do not automatically lead to a "ruling out" of sprue-like enteropathy. Similarly, when he testified that he would not find abdominal pain to be a "very plausible case of sprue-like enteropathy," his answer did not absolutely rule out sprue-like enteropathy as a possible diagnosis. In fact, his reasoning was that there are "more definite and less definite cases," with abdominal pain being an example of a "less definite" case of sprue-like enteropathy. Certification of Daniel B. Carroll in Support of Reply to Motion to Exclude Dr. Stephen Lagana ("Carroll Cert."), Exhibit C, Deposition of Dr. Stephen Lagana ("Lagana Dep.") at 77:4-19.

Plaintiffs also take issue with Defendants' omission of four words from a portion of a testimony cited by Defendants, where Dr. Lagana agreed that "there is no cardinal finding which can establish the diagnosis of olmesartan-induced injury ***based solely on histopathology.***" *Id.* at 231:14-232:17 (emphasis added). Plaintiffs attempt to explain that "based solely on histopathology" demonstrates that clinical context "is an important part of differentiating in an individual patient." Pls.' Br. at 3 (Dkt. 1106). But this reasoning stands in stark contrast to Dr. Lagana's own testimony, where he made it clear that he does not know what clinical findings a

doctor needs to have before diagnosing a patient with sprue-like enteropathy. Carroll Cert. Exhibit C, Lagana Dep. at 76:5-77:2. Instead, he opts to leave it to the “judgment of the treating physician.” *Id.* at 77:1-2.

When further pressed on identifying the clinical criteria required to diagnose sprue-like enteropathy, Dr. Lagana testified that “there are varied clinical presentations and varied pathologic presentations; and, therefore, it requires the patient’s doctor to make a reasonable assessment based on the entire clinical picture.” *Id.* at 78:24-79:7.

In *Black v. Food Lion, Inc.*, the Fifth Circuit addressed the question of whether expert testimony regarding the causation of fibromyalgia by trauma was sufficiently reliable to be admissible. 171 F.3d 308 (5th Cir. 1999). After reviewing the materials submitted in support of the expert testimony, the Fifth Circuit determined that the testimony did not satisfy the *Daubert* factors for reliability. *See id.* at 313. It concluded that “neither [plaintiff’s expert] nor medical science knows the exact process that results in fibromyalgia or the factors that trigger the process. Absent these critical scientific predicates, for which there is no proof in the record, no scientifically reliable conclusion on causation can be drawn.” *Id.* at 314. The court held that the admission of the expert testimony was an abuse of discretion. *Id.* at 314-15. Likewise, Dr. Lagana’s inability to define sprue-like enteropathy or to identify the clinical parameters that distinguish it from

other conditions is fatal to his opinion and should be rejected.

Last, Plaintiffs' argument regarding Dr. Lagana's inability to define general causation is nonsensical. They claim that Dr. Lagana's opinion that olmesartan causes sprue-like enteropathy in "some patients" is the definition of general causation. That is not the correct definition. General causation requires evidence to show "whether a substance is capable of causing a particular injury or condition *in the general population.*" *In re Human Tissue Prods. Liabl. Litig.*, 582 F. Supp. 2d 644, 649 n.1 (D.N.J. 2008) (emphasis added); *see also In re Zolof (Sertralinehydrochloride) Prods. Liab. Litig.*, 176 F. Supp. 3d 483, 491 (E.D. Pa. 2016). When asked whether he had concluded that olmesartan resulted in sprue-like enteropathy in the general population, Dr. Lagana responded that he "wouldn't necessarily say in the general population." Carroll Cert. Exhibit C, Lagana Dep. at 21:18-22. This unilateral modification to the widely-accepted definition of general causation is improper and unacceptable, and should be rejected by the Court.

B. Dr. Lagana did not analyze the Bradford-Hill criteria to support his opinion.

Further undermining Dr. Lagana's methodology is his failure to conduct a Bradford-Hill analysis in his report. Dr. Lagana's report does not mention the Bradford-Hill criteria, either by that title or by any other reference. Simply stated, the criteria were not part of his analysis. Plaintiffs' contention that Dr. Lagana's familiarity with the Bradford-Hill criteria should be sufficient to conclude that he

used the criteria in his report does not fill the empty gap. An expert's self-proclaimed accuracy is insufficient to prove that his opinions are reliable and useful to the jury. *Black*, 171 F.3d at 311, *see also*, *Moore v. Ashland Chem. Co.*, 151 F.3d 269, 276 (5th Cir. 2009).

Plaintiffs are now trying to present an after-the-fact Bradford-Hill analysis to justify Dr. Lagana's conclusions. This should not be allowed. *Caraker v. Sandoz Pharm. Corp.*, 172 F. Supp. 2d 1046, 1049 n.5 (S.D. Ill. 2001) (excluding causation expert whose Bradford-Hill analysis appeared to be an "afterthought" designed to justify the expert's conclusions).

A Bradford-Hill analysis is an essential element of an admissible causation opinion. *Reference Manual on Scientific Evidence* (Fed. Jud. Ctr. 2d ed. 2000) at 374-79; *Amorgianos v. Nat'l R.R. Passenger Corp.*, 137 F. Supp. 2d 147, 168 (E.D.N.Y. 2001), *aff'd*, 303 F.3d 256 (2d Cir. 2002). As Plaintiffs' own expert Dr. Susan Hutfless acknowledged in her report, the Bradford-Hill criteria is a "commonly used and generally accepted methodology in epidemiology to assess causality for non-infectious exposure-outcome relationships." Certification of Daniel A. Carroll, Esq. in Support of Defendants' Motion to Exclude the Testimony of Plaintiffs' Expert Susan Hutfless, Ph.D. ("Hutfless Cert."), Exhibit A, Report of Dr. Susan Hutfless at 15.

If Plaintiffs were so confident that Dr. Lagana incorporated the Bradford-

Hill criteria in his report, they would have at least been able to cite to sections of his report that implicitly incorporated and considered the Bradford-Hill criteria - even under a different name or no name at all. But they have not; nor can they. Nowhere in his 24-page report does Dr. Lagana explicitly or implicitly consider and analyze the Bradford-Hill criteria, whether under the title of “Bradford-Hill” or as individual criteria.

Further, contrary to what Plaintiffs’ claim (Pls.’ Br. at 7, Dkt. 1106), Dr. Lagana was not just asked if the Bradford-Hill criteria were “mentioned” in his report. He was asked if they were “addressed” *or* “mentioned,” and his response was “no”: “Q. Those criteria are not addressed, not mentioned, in your report; correct? A. Not specifically, no.” Carroll Cert. Exhibit C, Lagana Dep. at 357:12-16. He also admitted that he has never “specifically written a paper in which [he] looked at each [Bradford-Hill] point and made a response.” *Id.* at 357:2-4.

Combined, these statements establish Dr. Lagana’s failure to analyze and incorporate the Bradford-Hill criteria into his report, and render his general causation opinion unsound and ungrounded in any reliable scientific methodology. *See Gannon v. United States*, 571 F. Supp. 2d 615, 640 (E.D. Pa. 2007) (rejecting general causation testimony by expert who admitted that Bradford-Hill criteria were not met), *aff’d*, 292 F. App’x 170 (3d Cir. 2008); *Miller v. Pfizer, Inc.*, 196 F. Supp. 2d 1062, 1078 (D. Kan. 2002) (excluding causation testimony of expert who

misapplied Koch's postulates, criteria comparable to the Bradford-Hill criteria), *aff'd*, 356 F.3d 1326 (10th Cir. 2004); *In re Breast Implant Litig.*, 11 F. Supp. 2d 1217, 1233 n.5 (D. Colo. 1998) ("Plaintiff's causation experts must still satisfy the additional Bradford-Hill criteria to establish scientific cause and effect. Plaintiff's experts have not addressed the Bradford-Hill criteria at all.").

Plaintiffs' reliance on *Glynn v. Merck Sharpe & Dohme Corp.*, 2013 WL 1558690 (D.N.J. Apr. 10, 2013) is misplaced because the expert in that case had explicitly relied on the Bradford-Hill criteria in his report. *Id.* at *6, Certification of Daniel B. Carroll, Esq. in Support of Opposition to Plaintiffs' Motion to Exclude Dr. Keith Wilson ("Wilson Cert."), Exhibit D. The *Glynn* court's comment regarding defendant being free to address the issues on cross-examination directly related to defendant's objections concerning an expert's reliance on studies that did not find causation. That is not the case here. Dr. Lagana has testified that he neither addressed nor mentioned the Bradford-Hill criteria in his report and does not know why he did not analyze them. Carroll Cert. Exhibit C, Lagana Dep. 357:5-24.

C. Dr. Lagana's failure to rule out other explanations for sprue-like enteropathy is fatal to his causation opinion.

As established in Defendants' opening brief, Dr. Lagana testified that alternative explanations for enteropathy need not be ruled out. Plaintiffs attempt to put Dr. Lagana's testimony into context by discussing Table 3 of the Mayo Clinic

article. That added context brings nothing new to Dr. Lagana's statement. Dr. Lagana's testimony on what a clinician should do before diagnosing sprue-like enteropathy is straightforward and speaks for itself. According to Dr. Lagana, it would be reasonable if a physician *did not* rule out other explanations for enteropathy before diagnosing sprue-like enteropathy associated with olmesartan. Although Dr. Lagana tried to validate his viewpoint on this issue by stating that there is a difference between what is "ideal" and what is "reasonable," his testimony was clear in which he found it reasonable for a physician to not rule out other possible alternatives.

CONCLUSION

For the foregoing reasons, Defendants respectfully submit that Dr. Lagana's general causation opinion should be excluded.

Respectfully submitted,

s/ Susan M. Sharko

Susan M. Sharko, Esq.

Michael C. Zogby, Esq.

Daniel B. Carroll, Esq.

DRINKER BIDDLE & REATH LLP

A Delaware Limited Liability Partnership

600 Campus Drive

Florham Park, New Jersey 07932-1047

(973) 549-7000

Attorneys for Defendants Daiichi Sankyo, Inc., Daiichi Sankyo US Holdings, Inc., Daiichi Sankyo Company, Ltd., Forest Laboratories, LLC, Forest Pharmaceuticals, Inc., and Forest Research Institute, Inc.

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